Symposium on Geriatric Endocrinology

Thyroid Dysfunction in the Elderly

Elizabeth Paz-Pacheco MD
Past President, Philippine Society of Endocrinology and Metabolism
Associate Professor, University of the Philippines College of Medicine
Editor-in-Chief, JAFES
Who are the Elderly?

- Different Age Cut-offs Worldwide
  - Developed Countries 65+ years
  - American Geriatrics Society 65+ years
  - African Countries 50+ years
  - WHO 60+ years
  - United Nations 60+ years
  - Philippines 60+ years
Elderly Sub-population

* Young Old 65 - 74
* Old 74 - 84
* Old Old 85+
Young Children and Older People as a Percentage of Global Population: 1950-2050

Growth of the Population Aged 65 and Older in India and China: 2010-2050

Declining Sex Ratio in a Woman’s World...

- Birth: 106 Men, 100 Women
- 20 - 29: 82 Men, 100 Women
- 65 - 74: 65 Men, 100 Women
- 75 - 84: 41 Men, 100 Women
- 85+: 41 Men, 100 Women
Elderly Population in the Philippines

Philippine Demographics 2014

National Statistics Office Data as of August 23, 2014
What is the “physiologic” consequence of aging on the thyroid-pituitary axis?

Does the clinical picture of hypo- or hyperthyroidism change with age?

How should the diagnosis be established?

Should subclinical forms be treated?

Is there a difference in the therapy for elderly patients with thyroid dysfunction?
Physiologic HPT Axis Changes with Aging

- **Reduced** TRH synthesis and release due to altered hypothalamic neuro-regulation
- **Normal** serum TSH
- **Increased** pituitary sensitivity but **Decreased** peripheral sensitivity to circulating thyroid hormones
- **Reduced** thyroid hormone secretion
- **Low** T3, **Normal** T4
- **Decreased** T4 degradation
- OVERALL = **Partial Central Hypothyroidism**
Relative hypothyroid state in aging → Energy conservation → Evolutionary Advantage

Elderly = Normal FT4, FT3, TSH

Abnormal thyroid function NEEDS to be investigated and explained
TSH distribution curve shifts to higher values in older adults.

Word of Caution about TSH

- **A single TSH measurement** that is just below or above the reference limits may be a transient deviation in approximately 50% of older patients.
- Thus, **treatment decisions should wait**, if clinically possible, until repeat determinations are made over time.
- **Studies on the relationship between subclinical thyroid disease and metabolic syndrome or cognitive function** still provide **inconsistent findings**.
Clinical symptoms are VAGUE
Symptoms commonly misinterpreted as "Normal aging"
Thyrotoxicosis → Minimal symptoms
Hypothyroidism → Non-specific symptoms
Clinical Diagnosis is DIFFICULT
Influence of age on the prevalence of symptoms of thyroid dysfunction

1. Thyrotoxicosis (n=84)

2. Hypothyroidism (n=121)

Prevalence of Thyroid Dysfunction in Asymptomatic Filipino Elderly

Holgado-Galicia MV, Ramos HC, Jimeno CA. Prevalence of Thyroid Dysfunction Among Asymptomatic Elderly Filipinos at the Philippine General Hospital. JAFES 2012;27(1):72-76
Treatment is INDICATED.

Hyperthyroidism
- Render patient euthyroid with anti-thyroid drugs
- RAI offered earlier
- Surgery still SAFE even for Age > 75

Hypothyroidism
- Start with LOW dose then slowly up-titrate dose
- Target TSH = Low normal
Subclinical Thyroid Disease in the Elderly

Subclinical Hyperthyroidism
Subclinical Hypothyroidism

Age, sex, dietary iodine intake and TSH cut-offs used to define normal range
Natural History of Subclinical Hyperthyroidism

Case : Subclinical Hyperthyroidism

- 76/M
- 10 year history of goiter not associated with any symptoms.
- Co-morbidities: Hypertension, Diabetes
- Clinically euthyroid
- (+) multiple thyroid nodules on both lobes
- Unremarkable systemic PE findings
- FT4 = 14.5 pM (N.V. 11-24 pM)
- TSH = 0.02 uIU/ml (N.V. 0.3-3.8 uIU/ml)
- Do we treat this patient?
Case: Apathetic Thyrotoxicosis

- 72/F → Behavioral Change
- Relatives noticed patient to have 3 months history of gradual loss of appetite and weight loss.
- Patient prefers to be alone and asleep most of the time.
- Consulted a psychiatrist given anti-depressant but no relief of symptoms hence referred to an internist
- Unremarkable PE findings except for an irregular heartbeat. (-) exophthalmos
- 12L ECG revealed atrial fibrillation
- FT4 = 34.8 pM (N.V. 11-24 pM)
- TSH = 0.01 uIU/ml (N.V. 0.3-3.8 uIU/ml)
Excess All Cause Mortality in Subclinical Hyperthyroidism

Subclinical $\rightarrow$ Overt Hyperthyroidism based on TSH Levels

Risk factor for Atrial fibrillation and heart failure and Osteoporosis in postmenopausal women

Increased mortality with suppressed TSH

Treatment reverses osteoporosis but NOT cardiac changes

Treatment INDICATED for TSH < 0.1 mU/l

Persistently low serum TSH concentrations and normal free T4 and free (or total) T3 concentrations

Assess with radioisotope imaging and consider doing a doppler thyroid sonogram with colour flow

Assessment shows subclinical hyperthyroidism is due to toxic multinodular goitre or solitary adenoma

Assessment shows subclinical hyperthyroidism is due to Graves' disease
Subclinical Thyroid Disease in the Elderly

Subclinical Hypothyroidism (4-20%)
Subclinical Hyperthyroidism (1/10 of subclin hypo)

Age, sex, dietary iodine intake and TSH cut-offs used to define normal range
Natural History of Subclinical Hypothyroidism

Case: Subclinical Hypothyroidism

- 82/F
- Routine yearly general check up
- Hypertensive, Asthmatic
- Good functional capacity
- Family doctor ordered thyroid function test
- FT4 = 19.2 pM (N.V. 11-24 pM)
- TSH = 4.6 uIU/ml (N.V. 0.3-3.8 uIU/ml)
- Unremarkable systemic PE findings
- Do we treat this patient?
69/F → Fatigue and Weight loss
Recalls to have episodes of palpitations and easy fatiguability 10 years ago which resolved spontaneously
6 months history of gradual weight loss, loss of appetite and frequent fatigue and malaise.
Patient appears sleepy most of the time.
Unremarkable PE findings except for a multinodular goiter
FT4 = 9.2 pM (N.V. 11-24 pM)
TSH = 11.4 uIU/ml (N.V. 0.3-3.8 uIU/ml)
Anti-TPO = 358 IU/ml (N.V. < 100 IU/ml)
Subclinical Hypothyroidism

* Normal T3 and T4 with elevated TSH (mostly <10 mU/L, occasionally 10-20)
* **Etiology:** autoimmune, external radiation etc (similar to younger individuals); obesity (leptin stimulating TRH and subsequently elevating TSH)
* “Mild hypothyroidism”
* ? Dilemma: screening and Rx
* **US NHANES:** TSH rise with age: 70-90 TSH 6-9 in 95th %ile (eg TSH of 6 in an 80 year old is NORMAL)
Most feel well and have **no symptoms**. Whatever symptoms others feel are equivalent to euthyroid age matched individuals.

Large studies have shown: **NOT associated with physical function, cognitive dysfunction, depression or anxiety** (Roberts et al, Annals of Int Med, 2006)

**Aged 70-79:** increased walking speed, a measure of fitness, compared to euthyroid controls (Simonsick et al, Arch Int Med, 2009)

**Lower mortality** compared to normal euthyroid controls (Gussekloo et al, JAMA 2004)
Potential CV Risk in Subclinical Hypothyroidism

- Decreased diastolic function with exercise
- Impairment in vascular smooth muscle relaxation and arterial stiffness? Clinical significance
- Associated dyslipidemia in smokers and with IR (Cooper, Lancet 2012)
- Meta-analysis: increased coronary risk for TSH >10 mU/l (Rodondi et al, JAMA 2010)
- Rx is beneficial in 40-70 years but not for >80 (Razvi et al, Arch Int Med 2012)
- Heart failure is more common in TSH 8-10 mU/l (Nanchen et al, JCEM 2012)
TSH distribution curve shifts to HIGHER values in older adults

Percentage of US Population with Abnormal TSH as a Function of Age

* **NO** evidence for cognitive, metabolic, cardiovascular and affective dysfunction\(^1\)

* Increased TSH and Low FT4 prolongs life\(^2,3\)

* Age shifts to higher TSH reference values

* Levothyroxine treatment is **NOT** indicated \(^4\)

* Close follow-up for TSH > 12.0 mU/l

3 van den Beld et.al. (2005) Thyroid hormone concentrations, disease, physical function and mortality in elderly men. J Clin Endocrinol Metab 90: 6403–6409
Subclinical Hypothyroidism in Elderly IMPROVES CV risks

Majority of subclinical thyroid dysfunction will **NORMALIZE** with time.

Subclinical thyroid dysfunction **DO NOT** increase mortality rates in elderly

### Subclinical Hypothyroidism and CV Risk Factors in Filipino Elderly

<table>
<thead>
<tr>
<th>Cardiovascular risk factor</th>
<th>Subclinical hypothyroid (%)</th>
<th>Euthyroid (%) N = 162</th>
<th>Chi-square (p value)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N = 12</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>6 (50)</td>
<td>59(36.42)</td>
<td>0.348</td>
</tr>
<tr>
<td>Hypertension</td>
<td>8 (66.67)</td>
<td>95(58.64)</td>
<td>0.585</td>
</tr>
<tr>
<td>IHD</td>
<td>0</td>
<td>18 (13.58)</td>
<td>0.172</td>
</tr>
<tr>
<td>CVD</td>
<td>0</td>
<td>10(6.17)</td>
<td>0.375</td>
</tr>
<tr>
<td>Heart failure</td>
<td>1 (8.33)</td>
<td>6(3.70)</td>
<td>0.431</td>
</tr>
<tr>
<td>Total cholesterol &gt; 200 mg/dL</td>
<td>6 (50)</td>
<td>106(65.43)</td>
<td>0.281</td>
</tr>
<tr>
<td>LDL &gt; 130 mg/dL</td>
<td>5 (41.67)</td>
<td>107(66.07)</td>
<td>0.089</td>
</tr>
<tr>
<td>Triglyceride &gt; 150 mg/dL</td>
<td>4 (33.3)</td>
<td>65(40.12)</td>
<td>0.643</td>
</tr>
<tr>
<td>HDL &lt; 40 mg/dL</td>
<td>6 (50)</td>
<td>49(30.25)</td>
<td>0.156</td>
</tr>
<tr>
<td>Smoking</td>
<td>0</td>
<td>10(6.17)</td>
<td>0.375</td>
</tr>
<tr>
<td>Overall cardiovascular risk</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 20% ten-year risk</td>
<td>3 (25)</td>
<td>17 (10.49)</td>
<td>0.128</td>
</tr>
<tr>
<td>&lt; 20% ten-year risk</td>
<td>9 (75)</td>
<td>145 (89.51)</td>
<td>0.532</td>
</tr>
</tbody>
</table>

Holgado-Galicia MV, Ramos HC, Jimeno CA. Prevalence of Thyroid Dysfunction Among Asymptomatic Elderly Filipinos at the Philippine General Hospital. JAFES 2012;27(1):72-76
Contemporary Management of Subclinical Hypothyroidism

* Serum TSH $\rightarrow$ 3.0 - 4.5 mU/L
  * (+) anti-TPO – **MONITOR** periodically
  * Pregnancy – **TREAT** if TSH value is at the upper normal limit

* Serum TSH $\rightarrow$ 5.0 – 9.0 mU/L
  * Greater CV risk factors for age < 65 $\rightarrow$ **TREAT**
  * Age 61 – 80 $\rightarrow$ **NO** benefit of treatment
  * Age > 85 $\rightarrow$ **LONGER** life without treatment

* Serum TSH $\rightarrow$ > 10.0 mU/L
  * **TREATMENT** generally beneficial

Persistently raised serum TSH concentration

- Serum TSH concentration of 5-9 mU/L
- Serum TSH concentration of ≥10 mU/L
Prevalence of nodules increases with age (40-60% US)
Malignancy rates 10% (similar to younger groups)
Prevent unnecessary surgery with appropriate FNA confirmation
Management of nodules: Routine L-T4 suppression is not recommended given that the benefits are uncertain and risks of iatrogenic hyperthyroidism; osteoporosis and cardiac dysrhythmias in this age group
Thyroid malignancy in elderly is considered more advanced, with increased recurrence rates, hence critical to treat properly

(Ajish and Jakumar, Review, Geriatric Thyroidology, 2012)
Studies from the laboratories on three continents agree that the TSH distribution shifts to higher levels with age, particularly in people > 60 years of age.

The implications of these findings are that the traditional TSH distribution curve and reference limits need to be revised for older patients.

In > 70 years of age, the upper reference limit is in the range of 7.5mIU/l, and it is estimated that many older patients currently diagnosed with SCHypo are likely euthyroid and need not be treated with thyroid hormone.

A single TSH measurement that is just below or above the reference limits may be a transient deviation in approximately 50% of older patients. Thus, treatment decisions should wait, if clinically possible, until repeat determinations are made over time.

Studies on the relationship between subclinical thyroid disease and metabolic syndrome or cognitive function still provide inconsistent findings.

Thyroid nodules increase in the elderly, appropriate malignancy treatment
Symposium on Geriatric Endocrinology

Thyroid Dysfunction in the Elderly

Elizabeth Paz-Pacheco MD
Past President, Philippine Society of Endocrinology and Metabolism
Associate Professor, University of the Philippines College of Medicine
Editor-in-Chief, JAFES